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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,552	06/21/2001	Michael W. Leviten	R-67	5854

7590 10/24/2003

DELTAGEN, INC.
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Menlo Park, CA 94025

EXAMINER	
PARAS JR, PETER	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,552	LEVITEN ET AL.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *1-7,9 and 11-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Applicati n Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's amendment received on 6/25/03 has been entered. Claims 8 and 10 have been amended. Claims 1-16 are pending. Claims 8 and 10 are under current consideration.

Election/Restrictions

Claims 1-7, 9, and 11-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

Drawings

The drawings received on 6/25/03 are approved.

Claim Objections

The previous objection to claim 10 has been withdrawn in view of the claim amendments.

Upon further consideration the following new grounds of rejection under 35 U.S.C. § 101 are set forth below:

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8 and 10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to a transgenic mouse whose genome comprises a disruption in a target gene, wherein the target gene is capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1, and wherein the mouse exhibits increased response latency during a hot plate test and increased time in the central region during an open field test.

The instant specification has contemplated that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a cerberus gene. The instant specification has further contemplated that disruption of the nucleotide sequence set forth in SEQ ID NO: 1 in a mouse will produce a phenotype related to cerberus. The instant specification has purported that such mice may be used to identify agents that modulate or ameliorate a phenotype associated with a disruption in SEQ ID NO: 1.

The instant specification has disclosed a transgenic mouse whose genome comprises a disruption in SEQ ID NO: 1, wherein the mouse exhibits a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test. The claims embrace such a mouse and a method of making the mouse. The instant specification has discussed that phenotypes (decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing,

an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test) exhibited by such a transgenic mouse could correlate to a disease or disorder. However, the evidence of record does not provide a correlation between a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test and any disease or disorder. Moreover, while the specification has purported that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a cerberus, the evidence of record has failed to provide a correlation between any cerberus related disease/disorder and a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test. The specification has provided general assertions that the claimed transgenic mice may be used to identify agents that affect a phenotype related to the mice.

As such, the asserted utility, for the transgenic mouse embraced by the claims, of screening agents that may affect a phenotype of said mouse as provided by the instant specification and encompassed by the claims, does not appear to be specific and substantial. The asserted utility does not appear specific and substantial to the skilled artisan since the evidence of record has not provided any suggestion of a correlation between any cerberus, a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the

number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test, and any disease or disorder. Since the evidence of record has not provided a correlation between a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test and any disease or disorder, the utility of identifying agents that affect a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test is not apparent. The evidence of record has not provided any other utilities for the transgenic mouse embraced by the claims that are specific, substantial, and credible.

The asserted utility of the transgenic mouse embraced by the claims is based on the expectation that disrupting the nucleotide sequence set forth in SEQ ID NO: 1 would result in a detectable phenotype in the mouse. The phenotype observed in the transgenic mice embraced by the claims is a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test. While the phenotypes exhibited by the claimed transgenic mouse are contemplated to be associated with a disease, the association of a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number

of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test with any disease has yet to be elucidated. In fact the art suggests that results obtained from behavioral studies, such as the open field and tail suspension tests, are greatly influenced by the genetic background of the tested mouse. Crabbe et al (Science, 1999, Vol. 284, pages 1670-1672) observed that laboratory environment and site, test conditions, and genetic strain of a mouse could influence the results of behavioral studies. See pages 1670-1671. With regard to the open field test, Crabbe reports that A/J mice were relatively inactive, while C57BL/6 mice were very active. Crabbe further reports that on average mice tested in Edmonton were more active than those tested in Albany or Portland. See page 1671, column 1, the first full paragraph. Crabbe discusses that such inconsistencies in test results can be responsible for observed behavioral phenotypes. Given the inconsistencies in behavioral test results, Crabbe concludes by cautioning that specific behavioral effects observed in mutant (knockout) mice should be not be uncritically attributed to genetic manipulations prior to repeating testing in different laboratories using different strains of mice, if possible. See page 1672, column 1, paragraphs 2-3. Regarding the tail suspension test (TST), Liu et al observed significant differences in duration of immobility with respect to gender and genetic background. Liu et al reported that female mice had longer duration of immobility than male mice in basal TST duration of immobility while male mice exhibited significant strain differences in immobility duration for both basal TST and imipramine response TST. Finally, Liu et al concluded such results suggested that the responses

on basal TST and the imipramine-mediated responses on TST are mediated by separate genetic pathways. See the abstract and throughout the entire document.

Therefore, the reference suggests a need to provide independent evidence of an association of a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test with a disease or disorder. However, neither the specification nor any art of record provides evidence of the existence of a correlation between a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test and a disease or disorder, leaving the skilled artisan to speculate and investigate the uses of the transgenic mouse embraced by the claims. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the transgenic mouse embraced by the claims. In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse embraced by the claims to be specific and substantial.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER